the hydroxy compound IX, oxidized on standing in the air to the ketone VIII.

6,6,11-Trimethyl-11-hydroxy-6,11-dihydrobenz(b)acridine (X).—A 1.0-g. (0.00356 mole) portion of VIII was extracted from the thimble of a Soxhlet apparatus into a 12 ml. of ether solution of methylmagnesium iodide made from 1.02 g. (0.0072 mole) of methyl iodide. The red colored complex was decomposed with a saturated ammonium chloride solution. From the ether solution 0.954 g. (91% yield) of crude tertiary carbinol X, m.p. 151–155°, resulted; recrystallized from petroleum ether, m.p. 156–158°; λ_{max} 231, 273, 294, 300, 307, 313, 321 mμ ($\epsilon \times 10^{-3}$, 48.6, 4.3, 3.9, 3.9, 4.9, 4.0, 6.3); γ_{OH}, 3606/31, $\gamma_{C=C \text{ and/or } C=N}$, 1625/28, 1600/30.

Anal. Calcd. for $C_{20}H_{19}NO$: C, 83.01; H, 6.62; N, 4.84. Found: C, 83.30; H, 6.55; N, 4.92.

6,6-Dimethyl-11-oximino-6,11-dihydrobenz(b)acridine (XI) was not obtained by the usual methods for preparing oximes. A solution of 0.698 g. (0.01 mole) of hydroxylamine hydrochloride and 2.37 g. of dry pyridine in 10 ml. of freshly prepared abs. ethanol was mixed with a solution of 1.0 g. (0.0036 mole) of VIII in 30 ml. of abs. ethanol and refluxed for 5 days during which time the alcohol and water were allowed to distil off slowly being replaced from time to time with fresh abs. ethanol. A 68% yield, 0.818 g., of crude oxime, m.p. 219–224°, was isolated; recrystallization from ethanol gave colorless flakes, m.p. 222–224°, λ_{max} 244.5 mμ (ϵ 40,800).

Anal. Calcd. for $C_{19}H_{16}N_2O_2$: C, 79.14; H, 5.59; N, 9.72. Found: C, 79.10; H, 5.58; N, 9.81.

Catalytic hydrogenation of the oxime XI with Raney nickel in ethanol at 45 lb./in.^{2} for 10 hours produced an oil from which no solid product was isolated.

LINCOLN, NEBR.

Incomplete?

[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES]

Alkaloids from *Apocynaceae*. III.[1] Alkaloids of *Tabernaemontana* and *Ervatamia*. The Structure of Coronaridine, A New Alkaloid Related to Ibogamine[2]

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Six representative species of the genera *Ervatamia* and *Tabernaemontana* were investigated. The alkaloids ibogamine (Id), voacangine (Ia) and voacamine, common to the genera *Tabernanthe* and *Voacanga*, were isolated. In addition to these, four other alkaloids are described: olivacine (alkaloid "205"), dregamine, tabernaemontanine and coronaridine (Ic). The latter is shown by saponification and decarboxylation to be carbomethoxyibogamine (Id). Dregamine and tabernaemontanine are examples of 2-acylindole alkaloids.

In pursuing the study of different members of the family *Apocynaceae*, we became interested in botanical relatives of the African hardwood *Tabernanthe iboga* Baill.[1] This plant is a source of numerous alkaloids which have been studied by pharmacologists as potential stimulants.[4] The structures of these alkaloids have been elucidated by Taylor.[5]

Another genus closely related botanically to *Tabernanthe* is *Voacanga*.[6] The major alkaloid of *Voacanga africana*, voacangine (Ia), and that of *Tabernanthe iboga*, ibogaine (Ib), differ only in that the former contains an additional carbomethoxy function. The close relationship of these two alkaloids has been demonstrated by the conversion of voacangine to ibogaine.[7] While these two compounds are quite similar chemically, their pharmacology is different[8] in that voacagine lacks the stimulant properties of ibogaine.

Tabernanthe and *Voacanga* are close botanical relatives, being found in the same family: (*Apocynaceae*), subfamily (*Plumeroideae*) and tribe (*Tabernaemontanoideae*).[6]

In view of the structural correlations found among the constituents of these genera, it was of interest to investigate other members of the same tribe in the hope of finding biogenetically related alkaloids. Such alkaloids were present.[9]

The tribe *Tabernaemontanoideae* contains, according to Pichon,[10] twenty closely related genera. The largest of these are the genera *Tabernaemontana* with 140 species and *Ervatamia* with 92–96 species.[11] Of the remaining eighteen genera, eight are monotypic, and the rest range from two to twenty species.

We have chosen to investigate the two larger genera because of their broad distribution and availability. The following species were examined: *Ervatamia coronaria*, *E. divaricata*, *Tabernaemontana undulata*, *T. psychotrifolia*, *T. oppositifolia* and *T. australis*.

Ervatamia coronaria, syn. *Tabernaemontana coronaria*. This plant, an 8–10 foot tree, is cultivated throughout India both for the ornamental value of its fragrant white blossoms and as a medicinal. The leaves, bark and flowers of the plant are used in the Ayurvedic system for different ailments as a soothing agent.

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(1) Alkaloids from Apocyanaceae, II, Norbert Neuss, *J. Org. Chem.*, **24**, 2047 (1959).

(2) Presented in part before the Organic Division of the 139th National Meeting of the American Chemical Society, San Francisco, Calif., April, 1958.

(3) On leave from the University of Illinois as a trainee in the summer employment program, 1958, of Eli Lilly and Co., Indianapolis, Ind.

(4) J. A. Schneider, *Ann. N. Y. Acad. Sci.*, **66**, Art. 3 (1957), March 14, and references cited therein.

(5) W. I. Taylor, THIS JOURNAL, **79**, 3298 (1957).

(6) K. Schumann, in A. Engler and K. Prantl, "Die naturlichen Pflanzenfamilien," Vol. 4, part 2, 1895, p. 109

(7) F. Percheron, Alain Le Hir, R. Goutarel and M. W. Janot, *Compt. rend. acad. sci.*, **245**, 1141 (1957).

(8) R. C. Rathbun, Lilly Research Laboratories Pharmacology Division, private communication.

(9) After the presentation of these results, Walls, Collera and Sandoval reported the isolation, from the genus *Stemmadenia*, of the new alkaloids (+)-quebrachamine, isovocangine, stemmadenine, as well as the known alkaloids voacangine, voacamine, tabernanthine and ibogamine. These alkaloids are characteristic constituents of the genus *Voacanga*. The presence of these alkaloids in *Stemmadenia sp.* indicates the relationship of this genus to those of *Tabernanthe*, *Voacanga* and *Tabernaemontana* (*Tetrahedron*, **2**, 173 (1958)).

(10) M. Pichon, *Mem. Mus. Nat. Paris*, **24**, 111 (1948), *et seq.*

(11) In some species these genera are synonymous.

The isolation of alkaloids from this species has been reported by two groups.[12–14]

The earlier workers isolated two crystalline compounds, tabernaemontanine, a $C_{20}H_{26}O_3N_2$ compound, m.p. 208–210°, and coronarine, a yellow $C_{44}H_{56}O_6N_4$ compound, m.p. 196–198°.[12] The more recent investigation[13] yielded only tabernaemontanine of melting point 208–210°. Upon repeated recrystallization, the authors reported the substance as melting at 217–218°.

Since our material was grown in Florida by Menninger,[15] it was of interest to determine whether the alkaloidal constituents would be of the same nature as those found in the Indian material.

Total alkaloids obtained by the extraction of stems were chromatographed on deactivated alumina. Elution with benzene yielded small amounts of a new alkaloid called *coronaridine* which could not be induced to crystallize. Treatment of the base with ethereal hydrochloric acid yielded an amorphous hydrochloride which could be crystallized from acetone. Analytical results were in good agreement with its formulation as a $C_{21}H_{26}O_2N_2$ compound.

Further elution with a mixture of benzene-chloroform (3:1) yielded a second alkaloid, m.p. 207–209° (from ether). Recrystallization from methanol gave material melting at 217–219°. The double melting point of this alkaloid is in agreement with the melting points reported for the alkaloid *tabernaemontanine*.[12,13] Our analytical data for this compound do not exclude the possibility of its formulation as a $C_{21}H_{28}O_3N_2$ compound rather than $C_{20}H_{26}O_3N_2$ as postulated by the previous investigators.

Continuing the elution with the same solvent system yielded minute amounts of a new alkaloid called dregamine.[16]

Ervatamia divaricata.—This plant is classified by some authors as synonymous with *E. coronaria* and is commercially available in India.[17] Chromatography of the alkaloidal fraction yielded coronaridine as the only homogeneous material.

The following three species of *Tabernaemontana* were collected for us on Trinidad and neighboring islands where they are found both in natural and cultivated states.

Tabernaemontana undulata.—The results of a paper chromatogram of the alkaloidal fraction indicated the presence of at least three components. Repeated chromatography of this fraction has not yielded any crystalline material.

T. psychotrifolia.—The chromatography of the alkaloidal fraction obtained by the extraction of the root yielded upon elution with benzene coronaridine. The elution with benzene was then continued, yielding voacangine. Using benzene–chloroform mixtures (3:1), voacamine was obtained. Later fractions, eluted with the same solvent mixture, gave a small amount of a crystalline yellow alkaloid, olivacine.[18] The same alkaloid was obtained directly from the benzene extract of the plant by treating it with a tartaric acid solution, recrystallization of the tartrate and liberation of the free base.

This substance was shown to be a $C_{17}H_{14}N_2$ compound,[18] isomeric with ellipticine, also a yellow alkaloid, first isolated by Goodwin from *Ochrosia elliptica.*[19] The two compounds are characterized by very similar spectral and chemical properties. Thus, alkaloid "205" forms a methiodide which can be readily reduced with sodium borohydride to the corresponding tetrahydro compound.[20]

T. oppositifolia.—Chromatography of the alkaloidal fraction prepared from the benzene extract of the root yielded several known alkaloids. Elution with benzene gave first crystalline ibogamine, (Id)[6] then coronaridine, and, finally, voacangine. After elution with benzene–chloroform (1:1), voacamine was obtained.

T. australis.—This species was collected for us in northeastern Argentina. The alkaloids obtained were chromatographed to give voacangine, followed by voacamine.

The results described above are summarized in Table I.

The occurrences of the three alkaloids coronaridine (Ic), voacangine (Ia) and ibogamine (Id) in the same plant species (Table I) indicated a possible biogenetic relationship in their structures. An examination of the infrared spectra of the above alkaloids confirmed this speculation. The bands present in voacangine (Ia) and absent in coronaridine (Ic) could be attributed to a 5-methoxy indole moiety ($\lambda_{\max}^{CS_2}$ 6.15, 9.65, 12.05, 12.55 μ)[21] while those present in coronaridine (Ic) and absent in ibogamine (Id) were characteristic of a carbomethoxy function ($\lambda_{\max}^{CS_2}$ 5.8 μ, 8.05 μ).

TABLE I

ALKALOIDS ISOLATED FROM SPECIES OF *Ervatamia* AND *Tabernaemontana*

	Alkaloids			
Plants	Coronaridine	Voacangine	Voacamine	Others
E. coronaria	+	−	−	Tabernaemontanine Dregamine
E. divaricata	+	−	−	
T. undulata	−	−	−	
T. psychotrifolia	+	+	+	Olivacine (alkaloid "205")
T. oppositifolia	+	+	+	Ibogamine
T. australis	−	+	+	

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[12] A. N. Ratnagiriswaran and K. Venkatochalom, *Quart. J. Pharm. and Pharmacol.*, **12**, 174 (1939).

[13] S. A. Warsi and Bashin Ahmed, *Pakistan J. Sci.*, **1**, 128 (1949).

[14] S. P. Raman and A. K. Barua, *J. Indian Chem. Soc.*, **34**, 912 (1957), have reported on the triterpene constituents of this plant.

[15] E. A. Menninger, "What Flowering Tree Is That?" *Stuart Daily News*, Stuart, Florida, 1956.

[16] Dregamine was isolated as the main component of an alkaloidal extract prepared from the bark of the trunk of *Voacanga dregei* E. M.; N. Neuss and N. J. Cone, *Experientia*, **15**, 414 (1959).

[17] United Chemical Co. Ltd., Calcutta, India.

[18] This alkaloid was first thought to be a new compound and was referred to as alkaloid "205."[2] It has recently been identified as olivacine, reported by Schmutz from *Aspidosperma olivaceum* M. Arg. (J. Schmutz and F. Hunziker, *Pharm. Acta Helv.*, **33**, 341 (1958)). We should like to thank Dr. Schmutz for the direct comparison of our sample with that of authentic olivacine.

[19] Sidney Goodwin, A. F. Smith and E. C. Horning, THIS JOURNAL, **81**, 1903 (1959).

[20] We should like to thank Dr. Goodwin for experimental conditions for the preparation of these derivatives prior to the publication of her results.

[21] N. Neuss, H. Boaz and J. W. Forbes, THIS JOURNAL, **76**, 2463 (1954).